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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/244,130	02/04/99	DUJON	B 3495.0111-10

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EXAMINER	
KAUSHAL,S	
ART UNIT	**PAPER NUMBER**
1633	8

DATE MAILED: 06/05/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/244,130	DUJON et al
Examiner	**Group Art Unit**
SUMESH KAUSHAL	1633

☒ Responsive to communication(s) filed on *Jan 27, 2000*

☒ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *23-47* is/are pending in the applicat

Of the above, claim(s) _____ is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *23-47* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Double Patenting

1. Applicant's arguments filed 01/27/00 (page-1) have been fully considered but they are not persuasive. Applicant argues that the rejection be held in abeyance until allowable subject matter is indicated.

Claims 23-24, 27, 28, 31-32 and 39 are remain rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 15, 18, 21, 28 of copending Application No.08/643732 and is repeated for the same reasons of record as set forth in the official action mailed 10/26/99. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 15 and 28 of 08/643,732 are drawn to a non-human transgenic animal comprising a cell comprising an I-SceI site which encompasses the subject matter of claims 23, 24, 27 and 28 of instant application. Claim 18 ('732) is drawn to recombinant mouse or cultured cells comprising I-SceI site which encompass the subject matter of claim 39 of instant application. Claim 21 ('732) is drawn to a method, providing cells containing I-SceI site, and adding I-SceI endonuclease and transfecting a gene of interest which encompasses the subject matter of claim 31-32 of instant application. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

2. Claim 23-47 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to **make and/or use** is repeated for the same reasons of record as set forth in the official action mailed 10/26/99.

Applicant's arguments filed 01/27/00 (pages 4-7) have been fully considered but they are not persuasive. Applicant argues that the method of making of a transgenic mice comprising nucleotide sequence encoding I-Sce-I does not require undue amount of experimentation.

The specification teaches insertion of I-Sce-I site via homologous recombination in mouse NIH3T3 fibroblast and mouse PCC7-s multipotent cell lines using viral vectors (page 64, para.3, page 67, table-1). Furthermore, the specification teaches genetic recombination, especially the homologous recombination in the making of transgenic yeast (page 3, para.1-2, example 1, 2 and 3). Based upon these results the specification merely speculated that "the method can also be used with transgenic animals" (page 85 para.1, para.3). The specification fails to disclose any transgenic animal comprising a nucleotide sequence encoding I-SceI wherein the I-SceI is introduced by homologous or non-homologous recombination. Applicant argues that generation of a transgenic mouse from D3 embryonic stem cells would require only routine experimentation. However, the applicant fails to point out where in the specification the generation of D3 embryonic stem cells encoding I-Sce-I is disclosed (response 01/27/00 page 5, line 6-8). The applicant further cited Robertson and Le Mouellic references in support that transfected embryonic stem cells can be used to make transgenic animals. In addition, the applicant cited Viville's reference which states that D3 line is an excellent embryonic stem cell line but admitted that creating a transgenic mice is not as easy task because technique is very long and there are many steps that often fails (response 01/27/00, page 6, line 3-9).

The state of art at the time of filing teaches that transgene expression and the physiological results of such expression in transgenic animals was not always accurately predictable. It is well known in the art that the level and the specificity of a transgene as well as the phenotype of the transgenic animal are greatly dependent upon the specific expression vector used. The individual gene of interest, promoter, enhancer, coding or non-coding sequences present in the transgene construct and the site of integration, are the important factors that govern the expression of a transgene (Well RJ, Theriogenology 45:57-68, 1996; see page 61, para.2). Furthermore, many biochemical pathways are plastic in nature which reflects the ability of the embryo to use alternative gene when the preferred gene is modified (Kappel et al. Current Opinion in Biotechnology 3:358-353 1992, page 550, col.1, para. 3-4).

In addition, genetic modulation via homologous recombination is highly unpredictable art which requires numerous step that often fails (Viville, in Transgenic Animals, Houdebine (eds), Harwood academic publishers, France. pp307-321, 1997). Embryonic stem (ES) cells are very sensitive to culture conditions and have natural tendency to differentiate, giving rise to unstable genome which render these cells unusable. Furthermore, homologous recombination remains a rare event and the injection of ES in the blastocyte is also unpredictable (Viville page 308).

The specification as filed fails to disclose a transgenic mice encoding Sce-I nucleotide sequence. Considering the unpredictability in transgenic art one skill in the art would require undue amount of experimentation to make and use the invention as claimed.

The specification only exemplified the retroviral infection of a mouse PCC7-s multipotent cell line using viral vectors and fails to disclose that implantation of any selected clone lead to the making of a trasgenic mouse or any other animals (page 64, para.3, page 67, table-1). It is not clear how a mouse multipotent cell line would results in the development of the any and all species of the

transgenic animals (as claimed). Furthermore, methods of claims 31-47 are not enabled because the method (as claimed) requires the use of cells obtained from a transgenic animal or a transgenic mouse.

In addition, for the reasons set forth above the making of transgenic yeast or transfection of mouse cells in vitro does not recapitulate the complexities involved in the making of any and all transgenic animals. Although, one skilled in the art would have been able to make the claimed genetic constructs, it would have required excessive and undue experimentation to make a transgenic mice or any and all transgenic animals, without a predictable degree of success because the specification only provide guidance to make a transgenic yeast or transfected mouse cells.

Conclusion

No claims are allowed.

3. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal Ph.D. whose telephone number is (703) 305-6838. The examiner can normally be reached on Monday-Friday from 8:00 AM to 4:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor John L. LeGuyader can be reached on (703) 308-0447. The fax phone number for the organization where this application or proceeding is assigned as (703) 308-2035. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the group receptionist whose telephone number is (703) 308-0196.

S. Kaushal, AU 1633

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